



Automated measurements of TDLU involution: towards automated prediction of breast cancer risk

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Background

Terminal duct lobular units (TDLUs) are the milk-producing structures in the breast, as shown in Figure 1. Acini are berry-shaped substructures of TDLUs. With the completion of child-bearing and physiological aging TDLUs involute, resulting in a reduction of the TDLU count, TDLU size and the number of acini per TDLU. Women with inhibited TDLU involution are more likely to develop breast cancer [1]. Figure 1 (A) shows a large TDLU with many acini and (B) shows a smaller TDLU with less acini. If both images came from women of a similar age, then (A) would have a larger breast cancer risk than (B). **A major bottleneck in studying TDLU involution in large cohort studies is the need for labor-intensive assessment of TDLUs. We developed an automated method to capture TDLU involution measures.**

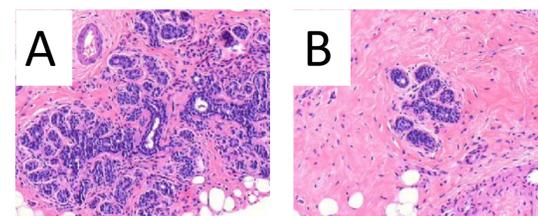
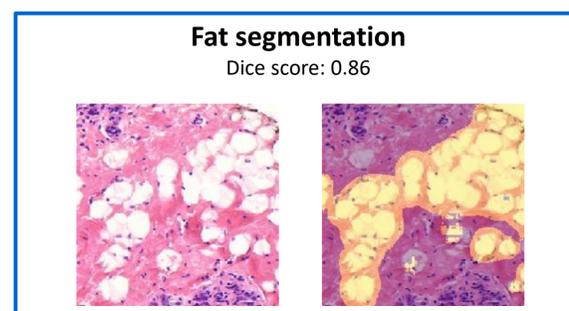
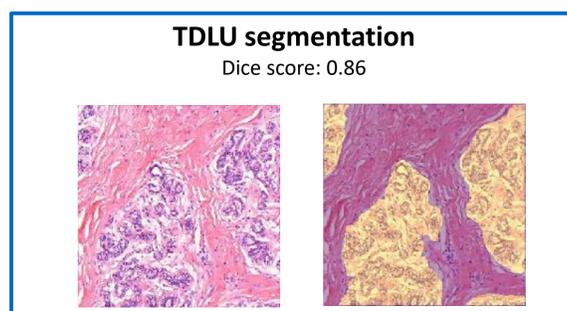
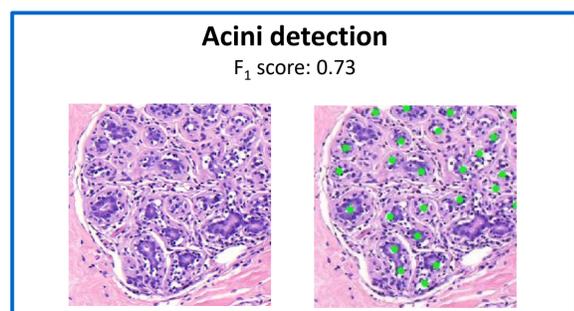


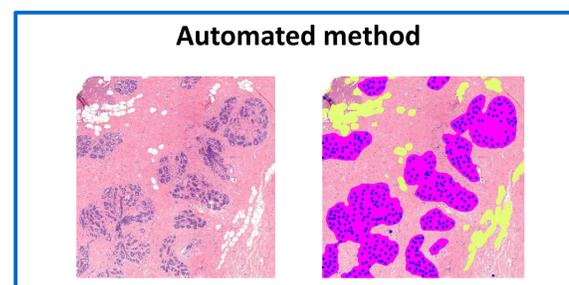
Figure 1: (A) A large TDLU with many acini, and (B) a small TDLU with few acini.

Methods

Whole slide images (WSIs) were obtained from the Nurses' Health Study (NHS). Ninety-two WSIs were annotated for TDLUs; a subset of 50 WSIs were also annotated for acini and adipose tissue. These annotations were used to **train networks with a U-Net architecture [2] for detection of acini [3], and segmentation of TDLUs and adipose tissue.**



These networks were integrated into **a single automated method to capture three proven TDLU involution measures [1,4]:** 1) number of TDLUs per tissue area (mm²), 2) median TDLU span (μm) and 3) median number of acini per TDLU. **We validated our method on 40 additional WSIs by comparing with manually acquired measures.** The correlation between manual and automated assessment was calculated using ICC and the association of TDLU involution measures with age was calculated using Pearson's correlation coefficient.



Results

Our CNN models detected acini with an F₁ score of 0.73 and segmented TDLUs and adipose tissue with Dice scores of 0.86 and 0.86, respectively. As shown in Table 1, the inter-observer ICC scores for manual assessments on 40 WSIs of number of TDLUs per tissue area, median TDLU span, and median acini count per TDLU were **0.71, 0.81, and 0.73**, respectively. Inter-observer ICC scores between automated results and the mean of the two observers were **0.85, 0.69 and 0.73**, respectively. TDLU involution measures evaluated by either manual or automated assessment were inversely associated with age (p<0.05).

Table 1: Inter-observer intra-class correlation coefficient (ICC) scores for the TDLU involution measures obtained from two observers and the automated method. The ICC was evaluated using 40 cases.

Inter-observer ICC scores	Pathologist 1 vs 2	Mean(pathologists) vs automated method
TDLUs per tissue area (adjusted for fat)	0.71	0.85
Median TDLU span	0.81	0.69
Median number of acini per TDLU	0.73	0.73

Conclusion

We developed an automated method to measure TDLU involution. **This technology eliminates the labor-intensiveness and subjectivity of manual TDLU assessment, and will be applied to a large epidemiological research cohort (NHS) for a future breast cancer risk study.**

Acknowledgements

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References

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